Diabetes drugs associated with fewer adverse cardiac events in older veterans

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GLP1 receptor agonists—a class of diabetes medications—are associated with fewer major adverse cardiovascular events than another type of diabetes drug (DPP4 inhibitors) in older veterans with no prior

heart disease. The findings, reported in *Annals of Internal Medicine*, will aid clinicians in choosing a diabetes drug regimen for older patients.

"We believe this study is an important contribution to patient care and adds to what we as clinicians know about treating diabetes and heart disease prevention," said Christianne Roumie, MD, MPH, professor of Medicine in the Division of General Internal Medicine and Public Health and senior author of the study.

More than 30 million adults in the United States have diabetes mellitus, and this diagnosis increases risk for adverse cardiovascular events (heart attack, stroke or cardiovascular death) and heart failure hospitalization, noted Lee Richardson, MD, a fellow in the Division of Cardiovascular Medicine and first author of the new study.

The researchers sought to address two knowledge gaps, Richardson said, first, that many newer diabetes medications were tested versus a placebo, making it difficult to know if one type offers an advantage over another, and second, that the clinical trials showing cardiovascular benefits for these drugs were conducted in people who already had heart disease.

"We wanted to see if there were differences in MACE—major adverse cardiovascular events—when comparing two commonly used drug classes, GLP1 receptor agonists and SGLT2 inhibitors, versus an active comparator, DPP4 inhibitors, in people without heart disease," Richardson said.

DPP4 inhibitors are regarded as neutral with respect to cardiovascular events and continue to be widely used, he added.

In a retrospective cohort study of U.S. veterans, the researchers found addition of a GLP1 receptor agonist was associated with about a 20% reduced risk of MACE and heart failure hospitalization, compared to

treatment with a DPP4 inhibitor in patients with Type 2 diabetes and no prior heart disease. The reduced risk translates to about three fewer heart failure, death, heart attack or stroke events in 1,000 people using the medication for a year, Roumie said.

SGLT2 inhibitors did not reduce MACE and heart failure hospitalization compared to DPP4 inhibitors for primary heart disease prevention.

The study included nearly 100,000 veterans who received a first prescription for an antidiabetic medication (metformin, insulin or sulfonylurea) from 2001 to 2016, and then added a GLP1 receptor agonist, SGLT2 inhibitor or DPP4 inhibitor to their diabetes treatment regimen. Follow-up data was collected through 2019.

The median patient age was 67 years, and the median diabetes duration was 8.5 years. The researchers included variables such as age, sex, race, body mass index, blood pressure, laboratory values like hemoglobin A1c, and history of prior illnesses in the statistical analysis.

The study did not examine the use of GLP1 receptor agonists, SGLT2 inhibitors or DPP4 inhibitors as first-line therapies for Type 2 diabetes treatment.

"Diabetes and its complications represent an enormous health care burden and result in nearly 200,000 deaths annually, often due to heart disease," Roumie said. "Doctors, scientists and patients want to do our best to prevent heart disease for those who are at highest risk. We believe that future primary prevention trials with these antidiabetic medications are needed. For some patients, these medications cost a lot, but if they prevent heart disease, then there would be a great return on investment."

Richardson noted that a limitation of the current study is that most of the

patients were white men.

"The hope for future primary prevention trials is that they would enroll a diverse cohort of participants who represent the patients we see in our clinics on a day-to-day basis," he said.

GLP1 receptor agonists include the medications exenatide, liraglutide, semaglutide and others; SGLT2 inhibitors include empagliflozin, dapagliflozin and canagliflozin; DPP4 inhibitors include alogliptin, linagliptin, saxagliptin and sitagliptin.

More information: Christianne Roumie et al, Comparative effectiveness of new hypoglycemic agents (SGLT2i and GLP1RA) on Primary Prevention of Major Adverse Cardiovascular Events: A National Retrospective Cohort of Older Veterans with Diabetes, *Annals of Internal Medicine* (2023). DOI: 10.7326/M22-2751

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